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EXAMINER	
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ART UNIT	PAPER NUMBER
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,156	YASUKOUCHI ET AL.	
	Examiner	Art Unit	
	Robert Shiao, Ph. D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/25/04,09/22/04,*. 3/14/06, 3/24/06
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the foreign application:

JAPAN 2001-395701 with a filing date 12/27/2001.

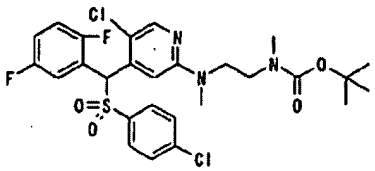
2. Amendment of claim 18 and addition of claim 34 in the amendment filed on November 20, 2006, is acknowledged. No new matter is found. Claims 18-34 are pending in the application. Since the newly added claim 34 is commensurate with the scope of the invention, claims 18-34 are prosecuted in the case.

Information Disclosure Statement

3. Applicant's Information Disclosure Statements, filed on June 25, 2004, September 22, 2004, March 14, 2006, and July 24, 2006 have been considered. Please refer to Applicant's copies of the 1449's submitted herein.

Responses to Election/Restriction

4. Applicant's election with traverse of Group III, in the reply filed on November 20, 2006, is acknowledged. Applicant's election of a species of Example 396,



i.e., is also acknowledged. During a telephone conversation with Paul J. Killos on January 23, 2007 a provisional election was made with traverse to prosecute the invention of Group I claims 18-33, in part (i.e., now are claims 18-34, in part), and the elected subject matter of Group I has been

discussed and modified as follows. The traversal is on the ground(s) that restriction is only proper if the claims of the restricted groups are either independent or patentably distinct, and the burden of proof is on the Office to provide reasons and/or examples to support any conclusions with regard to patentable distinctness, and M.P.E.P. 803 or 808.01(a) is cited. This is not found persuasive and the reasons are given *infra*.

Claims 18-34 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 18-34, in part, drawn to compounds/compositions of formula (3), wherein the variable R^{16} represents phenyl thereof; the variable R^{17} represents phenyl thereof; the variable R^{15} represents a heterocyclic group pyridyl thereof, and the optionally substitutent of monocyclic or polycyclic heterocyclic group of R^{15} is selected from piperazine, morpholine, piperidine, thiophene, or 1,3-dioxolane thereof, the variable R^{16}, R^{17} or R^{18} independently is not substituted with a heteroaryl, monocyclic or polycyclic heterocyclic group, and their processes of making and methods of use.

The claims 18-34 herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art, see Butlin et al. US 6,689,909. Butlin et al. disclose a similar compounds having a 6-membered heteroaryl ring (i.e., Formula (I)) as agents treating Alzheimer's disease, see columns 2-10. The instant claimed compounds of formula (3), wherein the variable R^{17} represents phenyl thereof, the variable R^{15} represents a heterocyclic group pyridyl thereof, which does not define a contribution over the prior art, as can be

seen by Butlin et al. US 6,689,909, see columns 2-10. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Furthermore, even if unity of invention under 37 CFR 1.475(a) is not lacking, which it is lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

> (1) A product and a process specially adapted for the manufacture of said product', or
>
> (2) A product and a process of use of said product; or
>
> (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
>
> (4) A process and an apparatus or means specifically designed for carrying out the said process; or
>
> (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

And, according to 37 CFR 1.475(c)

> if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

However, it is noted that unity of invention is considered lacking under 37 CFR 1.475(a) and (b). Therefore, since the claims are drawn to more than a product, and according to 37 CFR 1.475 (e)

> the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

The claims lack unity of invention and should be limited to only a product, or a process for the preparation, or a use of the said product. In the instant case, Groups I-

III are drawn to various products, processes of making and methods of use, and the final products do not contain a common technical feature or structure, and do not define a contribution over the prior art, i.e., a compound of claim 1, methods of use of claim 26. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner. Claims 18-34, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 18-34, in part, not embraced in above elected subject matter, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper and is maintained.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25, recites limitation "one or other ingredients", is indefinite and ambiguous. It is unclear what the "one or other ingredients" is. The range of "one or other ingredients" of claim 25 is from any prescription or non-prescription drugs. Such breath in view of the limited exemplification and the lack of scope of subject matter resulted from a search of the prior art indicated that the "scope" of claim 25 can not be

ascertained. In view of the high degree of unpredictability of the chemical art and "one or other ingredients" must be made available at the time the invention was made, i.e., filing of application, the broad scope can not be supplemented with future discovery of new "ingredients". It is recommended that "one or other ingredients" be limited to the specific disclosure. Dependent claims 26-27 are also rejected along with claim 25 under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter (i.e., one or more other ingredients) which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitation of "one or more other ingredients" of claim 25 is not found in the specification.

7. Claims 26-27 and 30-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using compounds of the formula (3) for treating Alzheimer's disease. The specification does not reasonably provide enablement of methods of use using compounds of the formula of claims 26-27 and 30-

32 for treating or preventing Down syndrome or diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 26-27 and 30-32 is intent methods of use using compounds of the formula (3) treating or preventing diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation. The instant methods of use are using compounds of formula (3), wherein the variable R^{15}

represents a heterocyclic group, which may have a substituent, R^{16} represents a cyclic hydrocarbon group which may have a substituent or a heterocyclic group which may have a substituent, R^{17} represents a cyclic hydrocarbon group which may have a substituent or a heterocyclic group which may have a substituent, R^{18} represents a hydrogen atom or a C1-6 alkyl group and X represents -S-, -SO- or -SO2-.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Butlin et al. '909 disclose a similar compounds having a 6-membered heteroaryl ring (i.e., Formula (I)) as agents treating Alzheimer's disease, see columns 2-10.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming intent methods of use using compounds of the formula (3) effective against diseases resulting from abnormal production or secretion of beta-

amyloid protein without limitation, which includes any diseases related to inhibition of abnormal production or secretion of beta-amyloid protein. As such, the specification fails to enable the skilled artisan to use the compounds of the formula (3) for treating or preventing Down syndrome or diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation. In addition, there is no proof that the claimed compounds of the formula (3) to treat or prevent Down syndrome or diseases other than Alzheimer's disease, in a human or to an animal model.

In addition, there is no established correlation between *in vitro* activity and accomplishing treating disorders or diseases related to all diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation, *in vivo*, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use the instant compounds since there is no description of an actual method wherein Down syndrome or any disorders related to all diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation in a host is treated or prevented.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the instant compounds of the claims due to the unpredictability of the treatment or prevention of disorders or disease related to all diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation. Down syndrome or diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation are known to have many obstacles that would prevent one of ordinary skill in the art from accepting treating or preventing regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of exemplary cell-based assay of inhibiting production of beta-amyloid protein, i.e., the inhibition of production of beta-amyloid protein in E35 cells in terms of EC_{50} values, see pages 650-654 of the specification. There are no *in vitro* or *in vivo* working examples present for the treatment of any diseases other than Alzheimer's diseases by the administration of the instant compounds of the instant invention. Down syndrome has been well known due to extra genetic material from chromosome 21. This extra material means that there are more gene expressed than normal, for example, overexpression of SOD1 gene, COL6A1 gene, ETS2 gene, etc., pleases visit Web site at http://www.emedicinehealth.com/down_syndrome/page3_em.htm. In the instant case, There are no *in vitro* or *in vivo* working examples present for the treatment of Down syndrome by modulation of those genes.

The breadth of the claims

The breadth of the claims is intent methods of use using the compounds of the formula (3) effective against all diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation. Furthermore, the instant claims cover "diseases" that are known to exist and those that may be discovered in the future, for which there is no enablement provided. Moreover, there is no reasonable basis for

assuming the instant compounds of formula (3) embraced by the claims will share the same physiological properties.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what disorders related to Down syndrome or a disease resulting from abnormal production or secretion of beta-amyloid protein without limitation would be benefited (i.e., treated or prevented) by the administration of the instant compounds of the formula (3), wherein the variable R^{15} represents a heterocyclic group which may have a substituent, R^{16} represents a cyclic hydrocarbon group which may have a substituent or a heterocyclic group which may have a substituent, R^{17} represents a cyclic hydrocarbon group which may have a substituent or a heterocyclic group which may have a substituent, R^{18} represents a hydrogen atom or a C1-6 alkyl group and X represents -S-, -SO- or -SO2- of the instant invention and would furthermore then have to determine which of the claimed methods of use using the instant compounds would provide treatment or prevention of disorders related to Down syndrome or a disease resulting from abnormal production or secretion of beta-amyloid protein without limitation, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to

determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of the instant claims for the treatment or prevention of Down syndrome or any diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation. As a result necessitating one of skill to perform an exhaustive search for which disorders related to a resulting from abnormal production or secretion of beta-amyloid protein without limitation, can be treated by what compounds of the formula (3), wherein the variable R^{15} represents a heterocyclic group which may have a substituent, R^{16} represents a cyclic hydrocarbon group which may have a substituent or a heterocyclic group which may have a substituent, R^{17} represents a cyclic hydrocarbon group which may have a substituent or a heterocyclic group which may have a substituent, R^{18} represents a hydrogen atom or a C1-6 alkyl group and X represents -S-, -SO- or -SO2-. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated or prevented by what compounds of the instant claims in order to practice the claimed invention.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds in regards to the treatment or prevention of the many diseases resulting from abnormal production or secretion of beta-amyloid protein without limitation, one

having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by deletion of "preventing" and incorporation of the limitation "Alzheimer's diseases" or "treating condition (i.e., in vitro)" into claims 26-27 and 30-32 respectively, would obviate the rejection.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-25, 28, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Anders et al. publication, Chemische Berichte, 1989, 122(1):105-11, also

see CAS:110:74541; or Traynelis et al. publication, Journal of Organic Chemistry, 1973, 38(25) :4334-9, also see CAS: 80:14814.

Applicants claim pyridyl compounds/compositions of formula (3), wherein the variable R^{16} represents substituted or unsubstituted phenyl thereof; the variable R^{17} represents substituted or unsubstituted phenyl thereof; the variable R^{15} represents a heterocyclic group pyridyl thereof, and the optionally substitutent of monocyclic or polycyclic heterocyclic group of R^{15} is selected from piperazine, morpholine, piperidine, thiophene, or 1,3-dioxolane thereof, the variable R^{16}, R^{17} or R^{18} independently is not substituted with a heteroaryl, monocyclic or polycyclic heterocyclic group, the variable X represents $-SO_2-$, -S- or -SO-, or its salt, see claim 18. Dependent claims 19-25 and 28 further limit a number of variable, i.e., the variable X represents SO2 or SO, see claim 19.

Anders et al. disclose six pyridyl compounds or its salt , see RN: 87732-48-7, 116665-03-3, 116665-01-1, 116665-09-9, 116665-10-2 and 116665-12-4.
They clearly anticipate the instant compounds of formula (3), wherein the variable R^{16} represents phenyl optional having a substitute (i.e., nitro or methyl) thereof; the variable R^{17} represents phenyl having a substitute (i.e. methyl); the variable R^{15} represents a heterocyclic group pyridyl thereof, the variable R^{18} represents a hydrogen atom or C_{1-6} alkyl (i.e., methyl), the variable X represents $-SO_2-$, or its salt (i.e., Na or Li).

Traynelis et al. disclose a pyridyl compounds, see RN:42362-48-1, which clearly anticipate the instant compounds of formula (3), wherein the variable R^{16} represents phenyl thereof; the variable R^{17} represents phenyl having a substitutes (i.e. nitro); the

variable R^{15} represents a heterocyclic group pyridyl thereof, the variable R^{18} represents C_{1-6} alkyl (i.e., methyl), the variable X represents -S-.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

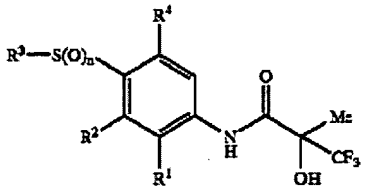
not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 18-34 are rejected under 35 U.S.C. 103(a) as being obvious over Butlin et al. US 6,689,909. Butlin et al. '909 is 102 (e) reference.

Applicants claim pyridyl/phenyl compounds/compositions of formula (3), wherein the variable R^{16} represents substituted or unsubstituted phenyl thereof; the variable R^{17} represents substituted or unsubstituted phenyl thereof; the variable R^{15} represents a heterocyclic group pyridyl thereof, and the optionally substitutent of monocyclic or polycyclic heterocyclic group of R^{15} is selected from piperazine, morpholine, piperidine, thiophene, or 1,3-dioxolane thereof, the variable R^{16}, R^{17} or R^{18} independently is not substituted with a heteroaryl, monocyclic or polycyclic heterocyclic group, the variable X represents $-SO_2-$, -S- or -SO-, or its salt, see claims 18 and 34 respectively. The instant compounds/composition of formula (3) are agents for treating Alzheimer's diseases, see claims 26-27 and 29-33. The administrating unit dose of the instant compounds/compositions is at a range of 0.5-100 mg/kg, see page 58 of the specification. Dependent claims 19-33 further limit a number of variable, i.e., the variable X represents SO2 or SO, see claim 19.

Determination of the scope and content of the prior art (MPEP §2141.01)

Butlin et al. disclose analogue pyridyl/phenyl compounds/compositions of formula (I),

i.e.,  , wherein the variable C represents pyridyl, the variable R^3 represents 6-memberredring heteroaryl (i.e., pyridyl) substituted with C_{1-6} alkyl, and the variable n is 1-2. Butlin et al. compounds are agents for treating Alzheimer's diseases, and the administrating unit dose at a range of 1-100 mg/kg, see columns 2-10 and 29.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Butlin et al. is that Butlin et al. do not disclose a species which anticipates the instant compounds of formula (3). However, Butlin et al. compound are analogue compounds having pyridyl/phenyl moieties for treating Alzheimer's diseases.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

Therefore, guided by the compounds of Butlin et al. one skilled in the art would expect all the compounds disclosed by Butlin et al. and their inherently teachings to have expected activity, i.e., treating Alzheimer's diseases. Therefore, a prima facie case of obviousness has been established against the instant application. It is well-established that consideration of a reference (i.e., Butlin et al. US 6,689,909) is not limited to the preferred embodiments or working examples, but extends to the entire

disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to person of ordinary skill in the art, see *in re Boe*, 355 F.2d 961, 148 USPQ 507, 510 (CCPA 1966); *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 279, 280 (CCPA 1976). Therefore, absent a showing of unobvious or unexpected results of the instant compounds of formula (3) in terms of physiological benefits or characteristics, the instant claimed compounds/compositions of known compounds would have been suggested to one skilled in the art. Dependent claims 19-33 are also rejected along with claim 18 under 35 U.S.C. 103(a).

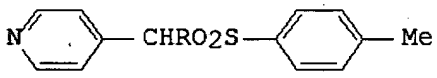
The motivation to make the claimed compounds derives from the expectation that the instant claimed compounds/compositions derived from known Butlin et al. compounds/compositions or their isomers and would possess similar activity (i.e., agents for treating Alzheimer's diseases) to that which is claimed in the reference.

11. Claims 18-34 are rejected under 35 U.S.C. 103(a) as being obvious over Anders et al. CAS: 110:74541 in view of Butlin et al. US 6,689,909. Butlin et al. '909 is 102 (e) reference.

Applicants claim pyridyl/phenyl compounds/compositions of formula (3), wherein the variable R^{16} represents substituted or unsubstituted phenyl thereof; the variable R^{17} represents substituted or unsubstituted phenyl thereof; the variable R^{15} represents a heterocyclic group pyridyl thereof, and the optionally substitutent of monocyclic or polycyclic heterocyclic group of R^{15} is selected from piperazine, morpholine, piperidine, thiophene, or 1,3-dioxolane thereof, the variable R^{16}, R^{17} or R^{18} independently is not

substituted with a heteroaryl, monocyclic or polycyclic heterocyclic group, the variable X represents -SO_2-, -S- or -SO-, or its salt, see claims 18 and 34 respectively. The instant compounds/composition of formula (3) are agents for treating Alzheimer's diseases, see claims 26-27 and 29-33. The administrating unit dose of the instant compounds/compositions is at a range of 0.5-100 mg/kg, see page 58 of the specification. Dependent claims 19-33 further limit a number of variable, i.e., the variable X represents SO_2 or SO, see claim 19.

Determination of the scope and content of the prior art (MPEP §2141.01)

Anders et al. disclose analogue pyridyl/phenyl compounds/compositions of Formula (I), i.e., 

, wherein the variable R represents Ph, C6H4NO_2-4, or tosyl.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Anders et al. is that the instant variable X represents SO_2 or SO or S, while Anders et al. represents SO_2 at the same position. Anders et al. compounds of formula (I) overlap with applicants' instantly claimed invention of formula (3).

Butlin et al. '909 compound are analogue compounds of instant compounds/compositions of fomula (3) having pyridyl/phenyl moieties for treating Alzheimer's diseases.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 18-34 prima facie obvious **because** one would be motivated to employ Anders et al. compounds and Butlin et al. compounds/composition and inherently teachings (e.g., agents of treating Alzheimer's diseases) to obtain the instant compounds/compositions of formula (3), wherein the variable R^{16} represents substituted or unsubstituted phenyl thereof; the variable R^{17} represents substituted or unsubstituted phenyl thereof; the variable R^{15} represents a heterocyclic group pyridyl thereof, and the optionally substitutent of monocyclic or polycyclic heterocyclic group of R^{15} is selected from piperazine, morpholine, piperidine, thiophene, or 1,3-dioxolane thereof, the variable R^{16}, R^{17} or R^{18} independently is not substituted with a heteroaryl, monocyclic or polycyclic heterocyclic group, the variable X represents $-SO_2-$, or its salt.

The motivation to obtain the claimed compounds derives from known Anders et al. compounds would possess similar activities (i.e., agents of pharmaceuticals for treating Alzheimer's disease) to that which is claimed in the reference.

Double Patenting

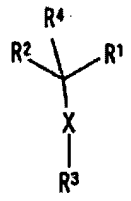
12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 18-34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 17 and 22 of Kubota et al. co-pending application No. 10/561,838. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

Applicants claim pyridyl/phenyl compounds/compositions of formula (3), wherein the variable R^{16} represents substituted or unsubstituted phenyl thereof; the variable R^{17} represents substituted or unsubstituted phenyl thereof; the variable R^{15} represents a heterocyclic group pyridyl thereof, and the optionally substitutent of monocyclic or polycyclic heterocyclic group of R^{15} is selected from piperazine, morpholine, piperidine, thiophene, or 1,3-dioxolane thereof, the variable R^{16}, R^{17} or R^{18} independently is not substituted with a heteroaryl, monocyclic or polycyclic heterocyclic group, the variable X represents $-SO_2-$, -S- or -SO-, or its salt, see claims 18 and 34 respectively. The instant compounds/composition of formula (3) are agents for treating Alzheimer's diseases, see claims 26-27 and 29-33. The administrating unit dose of the instant compounds/compositions is at a range of 0.5-100 mg/kg, see page 58 of the specification. Dependent claims 19-33 further limit a number of variable, i.e., the variable X represents SO2 or SO, see claim 19.



Kubota et al. claim compounds/compositions of formula (1), i.e., , wherein, R^1 and R^3 each independently represents an aromatic hydrocarbon group which may have a substituent an aromatic heterocyclic group which may have a substituent, R^2 represents a saturated or unsaturated monocyclic heterocyclic group or unsaturated polycyclic heterocyclic group which may have a substituent, R^4 represents a hydrogen atom or a C_{1-6} alkyl group, X represents -S-, -SO- or -S02-; an N-oxide or S-oxide thereof; a salt thereof; or a solvate thereof, see claim 1 and 17. Kubota et al.

compounds/compositions are agents for treating Alzheimer's disease, see claim 22.

The difference between the instant claims and Kubota et al. is that the variable R^2 represents a heterocyclic group, while the instant claims represent pyridyl at the same position. Kubota et al. compounds/compositions of formula (1) overlap with applicants' instantly claimed invention of formula (3).

One having ordinary skill in the art would find the instant claims 18-34 prima facie obvious **because** one would be motivated to employ Kubota et al. compounds/compositions and methods of use (e.g., treating Alzheimer's diseases) to obtain the instant compounds/compositions of formula (3), wherein the variable R^{16} represents substituted or unsubstituted phenyl thereof; the variable R^{17} represents substituted or unsubstituted phenyl thereof; the variable R^{15} represents a heterocyclic group pyridyl thereof, and the optionally substitutent of monocyclic or polycyclic heterocyclic group of R^{15} is selected from piperazine, morpholine, piperidine, thiophene, or 1,3-dioxolane thereof, the variable R^{16}, R^{17} or R^{18} independently is not substituted with a heteroaryl, monocyclic or polycyclic heterocyclic group, the variable X represents $-SO_2-$, -S- or -SO-, or its salt.

The motivation to obtain the claimed compounds derives from known Kubota et al. compounds/compositions would possess similar activities (i.e., treating Alzheimer's disease) to that which is claimed in the reference.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

14. Claims 18-34 are objected to as containing non-elected subject matter, i.e., heterocyclic group or heteroaryl, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on the pages 2-3 *supra*.

15. Claims 18 and 34 are objected as to because of the following informalities: A symbol of "(" or ")" is used for the limitation of variables R^{15}-R^{18}, i.e., see line 3 or 7 respectively. Replacement of the symbol "(" or ")" with a symbol "," would obviate the objection.

16. Claims 18-34 objected to as containing typographic errors. Replacement of the term "salt" with the term, "a salt", and replacement of the term "solvate" with the term, "a solvate" would obviate the objection. Replacement of the term "Alzheimer" with the term "Alzheimer's" of claims 27, 31 and 33 respectively would obviate the objection.

17. Claims 19-25, 28-29, and 32 objected to containing the term "of the above-described compound" under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert Shiao, Ph.D.
Patent Examiner
Art Unit 1626

January 25, 2007